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UPDATE

Importance of diagnosing optic nerve hypoplasia and the role of ophthalmologists

A Importância do diagnóstico da hipoplasia do nervo óptico e o papel do oftalmologista

La importancia del diagnóstico de la hipoplasia del nervio óptico y el rol del oftalmólogo

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ABSTRACT

The prevalence of optic nerve hypoplasia (ONH) has increased, and it is an important cause of visual impairment in childhood. As a diagnosis, ONH has been misunderstood because of its association with septo-optic dysplasia (SOD). ONH is a complex congenital disease of unknown etiology with a pessimistic visual prognosis. It is closely associated with hormonal changes in the hypothalamic–pituitary axis as well as with anatomic and functional changes in the brain, which lead to increased morbidity and mortality. Ophthalmologists are at a unique position to start the clinical investigation as soon as ONH is recognized and to refer the patient for complementary examinations and other medical specialties such that potentially necessary interventions are not delayed. The approach to ONH is multidisciplinary, and so are clinical interventions. The role of ophthalmologists includes the prescription of optical correction and aids, occlusion, and early visual stimulation at an appropriate age, which are all extremely important for the development and rehabilitation of affected children.

Keywords: Septo-Optic Dysplasia; de Morsier Syndrome; Hypopituitarism; Optic Nerve; Corpus Callosum.

RESUMO

Tem sido observado um aumento da prevalência da hipoplasia do nervo óptico (HNO) e a sua importância como causa de deficiência visual na infância. HNO, como diagnóstico, tem sido mal entendida por causa da sua associação com Displasia septo óptica (DSO). É uma doença congênita complexa de causa desconhecida, de prognóstico visual reservado e estreita associação com alterações hormonais no eixo hipotálamo-hipofisário e alterações cerebrais anatômicas e funcionais, com consequente aumento da morbimortalidade. O oftalmologista encontra-se na posição privilegiada de, assim que reconhecer a HNO, iniciar a investigação clínica, o encaminhamento para exames e para outras especialidades médicas, a fim de que as intervenções que se fizerem necessárias não sejam retardadas. A abordagem da HNO é multidisciplinar, assim como são as intervenções clínicas. No caso da oftalmologia, prescrição de correção óptica, oclusão, estimulação visual precoce e prescrição de auxílios na idade adequada são importantíssimos para habilitação/reabilitação das crianças.

Palavras-chave: Displasia Septo-Óptica; Síndrome de Morsier; Hipopituitarismo; Nervo Óptico; Corpo Caloso.

RESUMEN

Se ha observado un aumento del predominio de la hipoplasia del nervio óptico (HNO) y su importancia como causa de deficiencia visual en la infancia. La HNO, como diagnóstico, ha sido mal entendida a causa de su asociación con la Displasia septo óptica (DSO). Es una enfermedad congénita compleja de causa desconocida, de pronóstico visual reservado y estrecha asociación con alteraciones hormonales en el eje hipotálamo-hipofisario y alteraciones cerebrales anatómicas y funcionales, con consecuente aumento de la morbimortalidad. El oftalmólogo se encuentra en la posición privilegiada de, al reconocer la HNO, iniciar la averiguación clínica, el direccionamiento a los análisis respectivos y otras especialidades médicas, con la finalidad de que las intervenciones que se hagan necesarias no se retarden. El abordaje de la HNO es multidisciplinar, así como son las intervenciones clínicas. En el caso de la oftalmología, prescripción de corrección óptica, oclusión, estimulación visual precoz y prescripción de auxilios en la edad adecuada, son importantes para habilitación / rehabilitación de los niños.

Palabras Clave: Displasia Septo-Óptica; Síndrome de Morsier; Hipopituitarismo; Nervio Óptico; Cuerpo Calloso.

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INTRODUCTION

The prevalence of optic nerve hypoplasia (ONH) has increased, and it is an important cause of visual impairment in childhood[1]. As a diagnosis, ONH has been misunderstood because of its association with septo-optic dysplasia (SOD). Over the last decades, knowledge accumulated from several studies has proven that ONH is a neural development disease in childhood, which is associated with anatomic and functional changes in the brain and which leads to visual impairment and systemic and functional morbidity[1]. It is a complex congenital disease of unknown etiology, and it has a worse visual prognosis than do cerebral visual impairment, retinopathy of prematurity (ROP), and albinism[2]. ONH is not merely a component of SOD but rather an independent risk factor for hypothalamic–pituitary dysfunction. Due to its importance and because the absence of the septum pellucidum is only a casual finding, some authors consider ONH the main manifestation of that syndrome and propose that its name be changed to optic nerve hypoplasia syndrome or spectrum[2]. ONH is acknowledged to be a spectrum of central nervous system (CNS) diseases, manifesting as brain malformations, neurological deficits, and endocrine dysfunction[3].

DEFINITION

ONH is a non-progressive congenital disorder characterized by small optic discs, affecting one or both eyes[4,5]. Histologically, it is characterized by a subnormal number of optic nerve (ON) axons. It is a nonspecific manifestation of damage to the visual pathway that occurs before the latter is fully developed[5,6,7].

It is important to emphasize that ON morphology varies considerably in ONH[6]. The ophthalmologist is in the position to start the investigation and refer the patient for the diagnosis of associated changes[5,8].

The term "septo-optic dysplasia" (SOD)—a more frequent term—has been historically defined by changes in the brain midline, such as hypoplasia of the corpus callosum or the pituitary observed in nuclear magnetic resonance (NMR), ONH, and/or glandular changes in the hypothalamic–pituitary axis[9]. The presence of two manifestations of this triad defines the diagnosis. It is assumed that the abnormal development of the brain–forebrain midline must occur between the second and third month of pregnancy[10]. SOD is a clinically and radiologically heterogeneous disease in which cortical abnormalities are common, neurological development deficit is very prevalent, and clinical presentations are variable[11].

HISTORY

Knowledge regarding diseases in medicine is gathered by accumulating evidence that is first published in the form of case reports and later as a series of cases, followed by retrospective and prospective studies. This accumulation of knowledge leads to changes in definitions and even nomenclatures.

Morsier syndrome was so named by Hoyt et al. in an article published in 1970 that reported a series of 9 cases in which ONH was associated with growth hormone (GH) deficiency. In 4 of those cases, the septum pellucidum was absent. The authors attributed to Georges de Morsier the association of ONH with agenesis of the septum pellucidum[1,4,9]. However, Morsier (1956) had associated the absence of the septum pellucidum with several other ocular changes, which he collectively called "optic dysplasia," thus coining the term "septo-optic dysplasia" (SOD). In addition, Ellenberger and Runyan in 1970 described a case of unilateral ONH with absence of the septum pellucidum and dwarfism[1,4,9].

ONH was first described by Brière in 1877, and the first documentation of it with an artistic drawing was published by Schwarz in 1915[1,4,9]. ONH was first recognized as being associated with agenesis of the septum pellucidum by Dr. David Reeves in 1941[1,4,9]. In 1959, Gross and Hoff performed 465 autopsies of brains from patients with severe neurological problems or systemic malformations and reported a case of absence of the septum pellucidum with bilateral ONH. Moreover, they described a case of agenesis of the corpus callosum with unilateral ONH. Thus, only 2 cases of absence of the septum pellucidum with ONH had been described before 1970: one by David Reeves in 1941 and one by Gross and Hoff in 1959[1,4,9].

Since then, several studies have been conducted to better understand the causes and other characteristics of this complex disease.

In 1986, Morishima and Aranoff reported "atypical cases of SOD," without ocular lesions but with changes in structures of the brain midline and hypopituitarism or in areas other than the brain midline as well as with other clinical abnormalities[12].

In 2000, Miller et al. described SOD-plus, which is SOD associated with cortical malformation, particularly schizencephaly, with significant developmental delay and motor deficit[10]. Later publications have confirmed their finding[13].

In 2008, Borchert and Garcia suggested the name "optic nerve hypoplasia syndrome" based on the importance and predictive factor for the severity of a case when this ocular change is present[4]. In 2012, in a new review article, Borchert suggested that the terms "Morsier syndrome" and "septo-optic dysplasia" be deprecated[1].

PREVALENCE

ONH has been recognized as a frequent cause of congenital blindness, affecting one or both eyes, and its prevalence has increased over time[9]. It affects both sexes equally, although some publications have reported a greater incidence in males[6,7]. However, there are no studies reporting the preponderance of ONH in females[6].

It was estimated that ONH surpassed the prevalence of ROP as a cause of childhood blindness in Sweden in 1997, and in turn was only surpassed by cortical visual impairment[4]. At that time, the prevalence of SOD was 7.2 per 100,000 in Sweden, and in 2006, it was 10.9 per 100,000 in the United Kingdom[4]. A study on the prevalence of SOD in Europe has shown that it is more frequent in the United Kingdom than in mainland Europe[14]. In the United States, ONH was the third most frequent cause of visual impairment in children under 3 years of age in 2007, following cortical visual impairment and ROP[9].

In 2014, in New Zealand, ONH was found in 6.3% of the cases of severe visual impairment in children under 16 years of age[2].

A Canadian study reviewed medical records from 1986 through 2015 and observed a dramatic annual increase in the incidence of ONH/SOD, which was strongly associated with poverty and the Northern communities, leading to the hypothesis of an environmental and nutritional etiology[15].

In the last 40 years, the prevalence of ONH in the general population has increased nine-fold, now affecting 17.3 per 100,000 children under 18 years of age[3].

ONH appears to be more common and better recognized now than it was a few decades ago[7].

ETIOLOGY

The etiology of ONH is likely multifactorial involving a gene-environment interaction, whereby gene variants modify susceptibility to a toxic or beneficial product that influences the biologic response[1]. Thus, the pathogenesis of ONH reflects a combination of factors that lead to a temporal and spatial rupture of the genetic cascade responsible for early neuronal development during a period of vulnerability in the gestational window[1].

GENETIC CAUSES

The genetic mechanisms of the division of the forebrain into brain hemispheres and of the formation of the pituitary have been investigated in an attempt to explain the development failures that occur in ONH, defects of the brain midline, and endocrine dysfunctions[1,16].

A genetic mutation affecting the growth and transcription factors of the HESX1 gene has been reported, which leads to changes in ON development and in the formation of the anterior pituitary gland; however, this mutation is found in less than 1% of ONH cases[4,16]. Additionally, there are no reports of affected identical twins[9]. Another interesting fact is the very small number of families with more than one affected member as well as the absence of reported cases of transmission between generations[1].

There is no difference between the sexes, and there are few reported cases from Asian countries[4]. It is uncertain whether this is a sign of relative genetic protection, of environmental differences, or of cultural dietary differences.

The hypothesis of vascular change in the beginning of pregnancy could explain the anatomic changes in the midline and in ON[1,2,16].

GESTATIONAL HISTORY AND PRENATAL EXPOSURE

Several risk factors have been suggested, but some characteristics of the mother, such as being primipara and young, seem to be the most significant[1,2,4,9,14].

Two studies have suggested that bleeding during the first trimester of pregnancy may be a risk factor because this is more frequent in cases of ONH than in the general population[2].

Smoking during the first months of pregnancy also seems to increase the risk of ONH, which does not happen with drugs and alcohol[1,9].

The roles of lifestyle and nutrition are not well established[4]. Some studies have suggested that maternal weight loss or low weight gain in the prenatal period and premature labor (without premature birth) are additional risk factors[1,9].

ONH DIAGNOSIS

Diagnosis is clinical and made by direct ophthalmoscopy, which is considered the gold standard[1,4,9]. ONH is difficult to diagnose by indirect ophthalmoscopy because of the low magnification[1,9]. Morphometric techniques have been described based on photographs to measure either the disc area or diameter, but such techniques are usually impractical. In normal children, the ratio of the optic disc diameter (DD) and the distance between the temporal edge of the disc and the macula (DM) is greater than 0.35. A smaller value indicates ONH. In borderline cases, an optic disc that is at least 2 to 3 times wider than the central vessels of the retina is considered normal[4].

In premature children, a DD/DM ratio of 0.26 is considered normal[4].

There seems to be a spectrum comprising normal, atrophic, and hypoplastic optic discs, which depends on how severe the causal effect was and when it occurred[7].

The double-ring sign, either hypo- or hyperpigmented, is frequent[4,9]. This sign is presumed to be a view of the scleral canal that was covered as a result of the migration of the sensory retina or the pigment epithelium from the edge of the optic canal to that of the hypoplastic disc. It may appear in other ophthalmic conditions, such as myopia[9].

The vessels may be either tortuous or straight and without branching. The latter pattern has been recognized in children with primary GH deficiency[9].

ONH always coexists with some degree of chiasmal hypoplasia[7].

Anastasia et al. in 2015 have demonstrated the significant potential of diagnosing ONH using spectral-domain optical coherence tomography (SD-OCT). Changes have been detected in optic DD, in excavation depth, and in thickness of the retinal layers (thinning of the nerve fiber and ganglion cell layers). Foveal hypoplasia has also been observed. SD-OCT has been shown to have high sensitivity and specificity in detecting ONH[17].

CLINICAL ASSOCIATIONS OF ONH

Because the clinical picture can vary considerably, from mild to full manifestations, the incidence of ocular, cerebral, hormonal, and other forms of impairment may cause publication bias, depending on whether the focus is on ophthalmology, neurology, radiology, endocrinology, psychiatry, or pediatrics[12].

VISUAL IMPAIRMENT

Nystagmus usually appears between 1 and 3 months of age, whereas strabismus, usually esotropia, appears during the first year of life. In unilateral or asymmetrical ONH, strabismus may appear before nystagmus[1,4,9].

ONH is bilateral in 80% of the cases, and asymmetrical in two-thirds of the cases[1,4,9].

Bilateral ONH has a risk of pituitary dysfunction in 81% of the cases and a risk of developmental delay in 78% of the cases. Both risks are lower in cases of unilateral ONH.

Visual acuity is highly variable, but 80% of the cases of bilateral ONH are in the legal blindness range. Strabismic and anisometropic amblyopia may occur in association. It must be emphasized that the earliest clinical manifestation of ONH is poor visual behavior in a child[1].

Occlusion must be avoided in unilateral ONH and in very asymmetrical bilateral ONH[1,2,4].

In some children, visual acuity improves in the first years of life. It is believed that this is influenced by the myelinization of ON fibers. In cases associated with hypothyroidism, this improvement is infrequent[1].

Visual field changes are variable. Cecocentral scotoma, inferior altitudinal defect, defect contiguous to the blind spot, bitemporal hemianopsia, and homonymous hemianopsia have been described[5].

In unilateral cases and in those with significant asymmetry, Marcus Gunn pupil can be found[8].

HYPOTHALAMIC–PITUITARY DYSFUNCTION

This endocrine dysfunction affects most children with ONH regardless of the laterality and changes in neuroimaging of the septum pellucidum or the corpus callosum[1,3]. Hypopituitarism occurs in approximately 75% of the children with ONH and requires an early diagnosis and adequate management of pediatric patients[1,18].

HYPOPITUITARISM

All hormones may be affected by changes in the hypothalamus, the infundibulum, and the pituitary[4]. Hypopituitarism is believed to be due to hypothalamic dysfunction rather than pituitary dysgenesis[1,9].

GH deficiency is the most frequent (70%), followed by hypothyroidism (43%), adrenal insufficiency (27%), and diabetes insipidus (5%)[1,4,9].

Signals of absence of GH include hypoglycemia and prolonged jaundice with or without giant-cell hepatitis. GH deficiency leads to delayed tooth eruption, micropenis, delayed puberty, and short stature. However, cases of GH deficiency with ONH presenting normal growth rate have been documented[4].

Central hypothyroidism has been correlated to visual impairment at 5 years of age[1]. Central hypothyroidism is defined as a rupture of the hypothalamic–pituitary axis that leads to insufficient stimulation of the thyroid[19].

ACTH deficiency can lead to cardiovascular collapse in stressful situations and causes sudden death in 2% of the children with ONH[4].

Jaundice may be present in ACTH deficiency and hypothyroidism. The latter can also feature delayed puberty and growth[4].

ACTH and thyroid hormone are necessary for water excretion, and a deficiency of one or the both can lead to hyponatremia[1,4].

Hypopituitarism in children with ONH is usually associated with hyperprolactinemia[1]. Mild hyperprolactinemia occurs in 50% of ONH cases and is considered an auxiliary marker for hypothalamic dysfunction.

It is extremely important to note that the absence of hormonal deficiencies at a given moment does not imply the absence of future endocrine dysfunctions[4].

THIRST/HUNGER

Hyperphagia may occur, which is regulated by the lateral hypothalamic nucleus, causing obesity. Hypophagia may also occur, which is regulated by the ventromedial hypothalamic nucleus, with or without cachexia[1,4].

The ingestion of large quantities of water, resulting in polyuria, is common and may be mistaken for diabetes insipidus[1,4].

SLEEP

Circadian system disorders affect many children with ONH, probably due to inadequate retinal–hypothalamic input. Irregular sleep and waking patterns usually result in behavioral changes and often cause stress in the family[1,4].

TEMPERATURE REGULATION

Body temperature is regulated by the medial preoptic area of the hypothalamus, and this function is commonly affected in children with ONH. Temperature regulation problems in these children can lead to hospitalization to evaluate the possibility of sepsis[1,4].

GLUCOSE METABOLISM DISORDERS

Neonatal hypoglycemia may occur in some cases, and recurring hypoglycemia may lead to irreversible neurological damage[20]. Available studies emphasize that neonatal hypoglycemia is an important warning sign to suspect pituitary dysfunction. They also record a 2- to 6-year delay in SOD diagnosis in patients with visual and growth impairment even in cases with a history of neonatal hypoglycemia and a diagnosis of visual abnormalities in the first year of life[21].

NEUROPSYCHOLOGICAL DISORDERS

DEVELOPMENTAL CHANGES

Delayed development is common both in bilateral and unilateral ONH, with an estimated incidence between 71% and 75%. It ranges from an isolated focal defect to a global delay[1]. Motor development is affected in 75% of the cases, and communication in 44%. Hypoplasia of the corpus callosum, hypothyroidism, and bilateral ONH are considered risk factors[4,9].

AUTISM SPECTRUM DISORDER (ASD)

ASD occurs in approximately 25% of the children with visual impairment[9]. ASD appears to be more prevalent in children with ONH, but modifications in diagnostic tests for autism in visually impaired individuals are necessary for its real prevalence to be known[9]. Jutley-Nielson et al. recommend ASD assessment in all children with ONH and SOD, but for this assessment to be effective it will be necessary to create specific tests for visually and intellectually impaired children[22].

Williams et al. used two autism tests, systematically modified for children with a visual acuity of 20/800 or worse and observed that the results were encouraging[23].

OTHER SYSTEMIC, NON-ENDOCRINE ABNORMALITIES

Garcia et al. have reported in a 2006 retrospective study that non-endocrine systemic abnormalities occur in 47% of the children with ONH. These abnormalities include facial dimorphism, gastroesophageal reflux, malformations of the heart or great vessels, inguinal hernia, and hearing impairment. Gastroschisis, omphalocele, cleft palate, and cleft lip have also been reported in addition to other syndromes, such as Williams and Donnai–Barrow syndromes[2].

It is important to be aware of the disease as ONH can be found in patients with other systemic abnormalities and syndromes, and its diagnosis prevents delays in evaluation and treatment[2].

NEUROIMAGING

CORPUS CALLOSUM

The presence of hypoplasia of the corpus callosum, agenesis of the septum pellucidum, or pituitary malformation is highly suspicious, particularly when associated to a thinner ON in the images.

Retrospective and prospective studies have shown that in many cases, the agenesis of the septum pellucidum is incidental and not associated with ON or endocrine changes[9]. Moreover, it is not associated with ONH laterality, visual impairment, pituitary or growth changes[9].

Other NMR changes appear in less than 15% of the ONH cases: schizencephaly, cortical heterotopia, white-matter hypoplasia, pachygyria, holoprosencephaly, and arachnoid cyst[4].

Hypoplasia of the corpus callosum is the most prevalent neuroimaging abnormality associated with ONH, but the simultaneous occurrence of these changes is reported in less than 10% of the cases[1,9]. This change in the corpus callosum has been associated with developmental delay in children with ONH but not with hypopituitarism[1,9]. Other CNS abnormalities are present in 49% of the patients with hypoplasia of the corpus callosum, including defects that are unrelated to the midline and are typically associated to ONH (hydrocephalus, cortical heterotopia, pachygyria, schizencephaly, white-matter hypoplasia, polymicrogyria, and arachnoid cyst)[1,9]. Partial or total agenesis of the corpus callosum may also occur, and cardiopathy is more frequent in case of total agenesis of the corpus callosum (25%)[24].

Abnormal NMR findings are not predictive of endocrine dysfunction. Conversely, normal neuroimaging does not rule out the possibility of endocrine abnormalities[3,25]. However, such abnormal findings are risk factors for seizures and developmental delays[3].

PITUITARY GLAND

Pituitary neuroimaging abnormalities include empty sella, posterior ectopia, non-identification of the infundibulum, and posterior location of the pituitary. These abnormalities occur in 13% to 34% of the children with ONH[1,9]. In contrast, hypopituitarism occurs in 75% of the ONH patients, indicating that the absence of pathological neuroimaging of the pituitary does not rule out dysfunctions of that gland[9].

OPTICAL NERVE

High-resolution NMR can be used to distinguish ONH from optic atrophy, particularly because this technique can access the intracranial portion of ON[1,9].

Maresky et al. created a reference scale using NMR for measurements of ON (orbital and prechiasmatic), optic tract, and chiasma, correlated to five age ranges from 0 to 18 years[26]. The authors observed that the diameter of the visual pathway increased with age, with a positive correlation between ON and tract found for all ages[26].

OTHER FINDINGS

Hypoplasia of the pons, medulla oblongata, and vermis is significant and found in approximately 50% of the SOD cases[27].

The olfactory bulbs may be absent or hypoplastic[27].

CLINICAL MANAGEMENT

The physician must be vigilant of the signs of pituitary dysfunction and visual problems in children with ONH because this ON change rarely occurs in isolation[1,4,9]. A complete evaluation must be performed in every patient with ONH regardless of ON dimensions, visual acuity, or laterality[28].

Any child with prolonged jaundice, recurring hypoglycemia, and/or unstable temperature must undergo an ophthalmoscopic examination[1,2,16]. The same is indicated for children with nystagmus, strabismus, or poor visual behavior noticed before 3 months of age to rule out ONH.

If ONH is confirmed, the child should be referred for brain NMR and endocrine examination[4,9]. This is important not to merely identify the absence of the septum pellucidum but to detect treatable conditions, such as hydrocephalus, seizures, and focal deficits in schizencephaly or polymicrogyria, and to treat pituitary dysfunction[9]. Hypoplasia of the corpus callosum and other major malformations can anticipate developmental delay, allowing an earlier intervention to be planned[1].

The hormones to be assessed include morning cortisol, thyroid-stimulating hormone, free thyroxine (T4), GH and its substitutes, such as insulin-like growth factor 1 (IGF-1), and insulin-like growth factor-binding protein 3 (IGFBP-3)[1,9].

Luteinizing hormone, follicle-stimulating hormone, estradiol, and testosterone should be tested before 6 months of age and again at puberty, and micropenis (a sign of delayed puberty) can be treated with testosterone in childhood[1,2,9]. It must be stressed that puberty disorders are the least studied endocrine dysfunctions in ONH[29].

Prolactin must be evaluated after the sixth month of age[2].

It is important to note that normal pituitary function on the first evaluation does not rule out future endocrine dysfunction[1,4]. However, there is no consensus regarding the period for which a child should be monitored if hypothalamic–pituitary function is normal[2]. Prolonged follow-up is recommended due to reports of central hypothyroidism, subclinical GH deficiency, and association of untreated hypothyroidism with developmental delays and even death[29].

Growth and weight should be monitored every six months. A thyroid evaluation every six months should also be conducted in the first 3–4 years of life[1,4,9]. If growth slows down, GH should be measured, including a provocative test; thyroid, IGF-1, and IGFBP-3 evaluation should also be performed.

If the cortisol provocative test reveals a deficiency, glucocorticoid should be administered during an illness or physical stress.

Physiotherapy, speech therapy, occupational therapy, and early visual stimulation are required to improve language and feeding in children with ONH[1,4,9].

Melatonin can be used for sleep disorders.

Ophthalmological evaluation should be annual, and if necessary, spectacles and occlusion should be prescribed,4 but ophthalmologists must be aware that occlusion should be avoided in unilateral and in very asymmetrical bilateral ONH[1,2,4].

ASD management must be evaluated by a specialist, preferably one experienced with visually impaired children[1,4,9].

CONCLUSION

Management of ONH requires a multidisciplinary approach[4]. ONH is probably a non-hereditary condition, whose prevalence has been increasing and which leads to visual impairment. ONH can be considered a syndrome that includes hypothalamic, neuroanatomic, and developmental abnormalities. The absence of the septum pellucidum is of little importance for either the diagnosis or prognosis[9]. It is the presence of ONH that indicates the need for care measures, such as monitoring to anticipate the endocrine, systemic, and neurological abnormalities that are part of this condition[1].

Ophthalmologists are at a unique position to start the clinical investigation as soon as ONH is recognized and to refer the patient to complementary examinations and other medical specialties such that potentially necessary interventions are not delayed.

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